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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/586,235	06/02/00	HASAN T	10284016001

EXAMINER	
TRAN, M	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/586,235	HASAN ET AL.	
	Examiner	Art Unit	
	MAU T TRAN	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

This application is a Non-provisional application filed June 2, 2000 which claimed the benefit of application 60/137,365 filed June 3, 1999. An amendment to include an IDS was received on November 22, 2000 and entered. Claims 1-17 are pending.

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It was not executed in accordance with either 37 CFR 1.66 or 1.68.

The last inventor's signature appears to be a copy and not the original signature.

Specification

2. The use of the trademark photofrin has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

3. It is also noted that there are typos in the specification on page 19, line 19, the word "preformed" should be performed and on line 27, the word "efficiacy" should be efficiency. Correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting unwanted proliferation

in cells using photodynamic therapy (PDT) in combination with a cell differentiation factor in an ***in vitro*** cell culture system, does not reasonably provide enablement for treating a subject of unwanted cell proliferation using said method ***in vivo***. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 1-13 and 17 are drawn to a method of treating a subject having unwanted cell proliferation by inducing cell differentiation in combination with photodynamic therapy using chlorin derivatives as the photosensitizer.

In determining the enablement of the instant claims, some of the factors that were considered were 1) nature of the invention, b) state of the prior art, c) level of predictability, d) amount of direction given, e) existence of working examples, f) quantity of experimentation to make the invention.

It was disclosed in the specification that the claimed method has only been used on cell culture and in vitro (Figures 1-5). There is no working examples or guidance as to how to use this method to treat cancer in patients and no guidance as how to use this method to treat cancer in patients. The current state of the art show that this method has only been tried on cell culture and no data exists for use in patients or *in vivo* and the specification does not have enough guidance as to how to use the instant invention in an *in vivo* situation. It is well known in the art that cancer treatment in vivo is a complex process in which the individual's immune response and the host-tumor relationship have to be considered. To assume that all immune systems are alike would be naïve and the pathology, etiology and nature of the disease have to be considered individually (see Osband et al, Immunology Today, 1990, Vol. 11, pg. 193-195, specifically abstract and pg. 193, first column). Therefore, though a drug is able to work in an in vitro environment, it does not necessary guarantee the success of the therapy *in vivo* or that if the method of treating the cancer would even reach the tumor. The complexities of the human body is in no way represented by a petri dish and a cell culture and cannot be assessed without extensive experimentation.

One cannot extrapolate the teaching of the specification to the claims because it is well known that the art of anticancer drug discovery for cancer therapy is highly unpredictable, for example, Gura (Science, 1997, 278:1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second para). Because of the known unpredictability of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the method of treating cancer in patients by using a combination of photodynamic therapy with a differentiation factor would specifically kill cancerous cells and not other cells of the body.

Further, the refractory nature of cancer to drugs is well known in the art. Jain (Sci. Am., 1994, 271:58-65) teaches that tumors resist penetration by drugs (p.58, col 1) and that scientists need to put expanded effort into uncovering the reasons why therapeutic agents that show encouraging promise in the laboratory often turn out to be ineffective in the treatment of common solid tumors (p. 65, col 3). Curti (Crit. Rev. in Oncology/Hematology, 1993, 14:29-39) teaches that solid tumors resist destruction by chemotherapeutic agents and that although strategies to overcome defense mechanisms of neoplastic cells have been developed and tested in a number of patients, success has been limited and further teaches that it is certainly possible that cancer cells possess many as yet undefined additional molecular mechanisms to defeat chemotherapy treatment strategies and if this is true, designing effective chemotherapeutic regimens for solid tumors may prove a daunting task (para bridging pages 29-30) and concludes that knowledge about the physical barriers to drug delivery in tumors is a work in progress (p. 36, col 2). It is clear that based on the state of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the method of treating cancer in patients using PDT in combination with cellular differentiation factors would be successful in its specificity and potency.

However, there is no guidance in the specification for determining the appropriate time prior to the development of tumors to begin the therapy or for identifying patients at risk for developing those tumors. The specification provides insufficient guidance with regard to the issues raised above and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed methods with a reasonable expectation of success. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 10, 13 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7 recites the limitation "wherein a compound" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 10 recites "wherein the subject has and a PS and a retinoic acid, are administered to the patient." It is not clear what applicant is claiming as the instant invention. Clarification is required.

Claim 13 recites the limitation "wherein a tumor cell" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 16 recites the limitation "wherein the photosensitizer" in claim 14. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Momma et al (Int. J. Cancer, Vol. 72, pg. 1062-9, abstract).

Claims 14-15 are drawn to a method of detecting a cell having unwanted proliferation by providing a differentiating agent in combination with photodynamic therapy using a chlorin derivative as the photosensitizer.

Momma et al taught a method of treating prostate cell lines with photodynamic therapy PDT in combination with a cell differentiation factor (hormones) in the presence of protoporphyrin IX (PpIX), the same agent as disclosed by applicant to be the photosensitizer (Figures 1-5). Therefore, the reference anticipates the claims.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13 and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Momma et al (Int. J. Cancer, Vol. 72, pg. 1062-9) in view of Skalkos et al (US 5,424,305 1995, claims 2-15).

Claims 1-13 and 16-17 are drawn to a method of treating a subject or a cell of unwanted cell proliferation by treating cells with a differentiating factor in combination with photodynamic therapy using chlorin derivative as the photosensitizer.

Momma et al teaches a method of inhibiting prostate cell by treating the cell with a differentating factor in combination with photodynamic therapy and photosensitizer (PpIX) but differ from the instant claim of claim 16 by not disclosing chlorin and not using the method to treat cancer in patients.

Skalkos et al teaches porphyrins and its derivatives to include a method of using these compounds in treating bladder tumors but differ from the instant invention by failing to disclose a differentiating factor in this therapy.

However, it would have been *prima facie* obvious for one of the ordinary skill in the art, at the time the invention, was made to be motivated to combine the teachings of Momma et al and Skalkos et al to derive at the instant invention with a reasonable expectation of success. One would have been motivated to substitute any of the porphyrins in place of chlorins and its derivative as a photosensitizer because its function is similar to PpIX (US 5,424,305 column 1, last paragraph and abstract). Moreover it was suggested by Momma et al the method used in prostate cell treatment with differentiation factor in combination with photodynamic therapy should be considered in vivo (pg. 1068, column 1, last 2 lines and column 2, last line) because the combination therapy was effective against prostate cancer cell lines.

Conclusion

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mau Tran whose telephone number is 703-605-1165. The examiner can normally be reached on Monday-Friday from 8:00 a.m. – 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

GEETHA P. BANSAL
PRIMARY EXAMINER

Mau Tran, Ph.D.
Patent Examiner, Art Unit 1642
February 20, 2001